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## " YTP UPDATE 2020"

### OBESITY AND ANOVULATION

OBESITY IS THE GREATEST EPIDEMIC EVER EXPERIENCED BY HUMANS. IT SURPASSES ALL COMMUNICABLE DISEASES. IT IS NOW A GLOBAL HEALTH THREAT. SINCE 1980, THERE HAS BEEN A 27.5% INCREASE IN ADULT OBESITY AND 47.1% INCREASE IN CHILDHOOD OBESITY. ACCORDING TO INSTITUTE OF HEALTH METRICS AND EVALUATION AROUND 3.4 MILLION DEATHS ARE CAUSED BY OVERWEIGHT AND OBESITY. ACCORDING TO WHO 1 IN 3 CHILDREN ARE OVERWEIGHT OR OBESE. NO COUNTRY HAS REPORTED DECREASED OBESITY IN RECENT 33 YEARS.

THE IMPACT ON HEALTH DUE TO OBESITY RANGES FROM TYPE 2 DIABETES, HYPERLIPIDEMIA, OBSTRUCTIVE SLEEP APNOEA, CARDIAC DISEASE, HYPERTENSION, OSTEOARTHRITIS AND MANY MORE. THIS GLOBAL HEALTH ISSUE HAS A DETRIMENTAL EFFECT ON REPRODUCTIVE PHYSIOLOGY. WE NEED TO ANSWER IN WHAT WAYS CAN WE TACKLE THIS -PREVENTIVE AS WELL AS THERAPEUTIC AND ALSO WHETHER ACHIEVING A LIVE BIRTH IN OBESE WOMEN IS OUR PANULTIMATE GOAL.

OUR REPRODUCTIVE CONCERNS ARE MENSTRUAL IRREGULARITIES, OLIGO OR AMENORRHOEA, HEAVY MENSTRUAL BLEEDING, OVULATORY DYSFUNCTION, ALTERED OVARIAN RESPONSIVENESS, POOR OOCYTE QUALITY, MISCARRIAGES AND ADVERSE FOETO MATERNAL ENVIRONMENT . THE WHO CLASSIFIES OBESITY AS PER BMI.

UNDERWEIGHT - < 18.5

NORMAL- 18.5-24.9

OVERWEIGHT -25-29.9

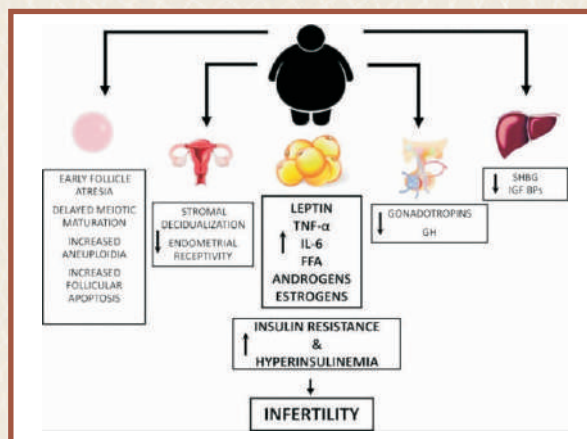
CLASS 1 OBESITY -30-34.9

CLASS 2 OBESITY-35-39.9

CLASS 3 OBESITY (EXTREME OR MORBID OBESITY) > 40

RELATIVE RISK OF OLIGOMENORRHOEA IN WOMEN WITH UPPER BODY FAT PREDOMINANCE IS 3.15(P<0.001) COMPARED TO WOMEN WITH LOWER BODY FAT PREDOMINANCE. THE "**CRITICAL BODY WEIGHT HYPOTHESIS**" GIVEN BY FRISCH et al SCIENCE 1970, STATES THAT THE CRITICAL BODY WEIGHT OF 47.8 KG AND A GREATER PERCENTAGE OF BODY WEIGHT CAN SERVE AS AN INITIATING SIGNAL. MENARCHE OCCURS AT A CRITICAL LEVEL OF FAT MASS CORRESPONDING TO 17% OF TOTAL BODY WEIGHT. OBESE PREPUBERTAL GIRLS ENTER MENARCHE EARLIER THAN NORMAL WEIGHT GIRLS. TO MAINTAIN OVULATORY CYCLES, A MINIMUM OF 22% FAT MASS OF TOTAL BODY WEIGHT IS REQUIRED.

#### PATHOPHYSIOLOGY



## LIPOTOXICITY

WHEN ENERGY INTAKE EXCEEDS THE CAPACITY OF NORMAL ADIPOSE TISSUE TO SAFELY STORE FAT, ECTOPIC LIPID ACCUMULATION OCCURS IN ADIPOSE CELLS. THIS EXCESS FREE FATTY ACIDS ACCUMULATES IN ABNORMAL LOCATIONS SUCH AS MUSCLE, LIVER ETC AND OXIDATIVE STRESS DEVELOPS IN THESE TISSUES WHICH LEADS TO INSULIN RESISTANCE AND INFLAMMATION. ASRM 2015 - LIPOTOXICITY AFFECTS GRANULOSA CELLS AND LEADS TO IMPAIRED OOCYTE MATURATION AND POOR OOCYTE QUALITY.

## OBESITY, ANOVULATION AND ENDOMETRIUM

- 1) CHRONIC ANOVULATION LEADS TO PROLONGED ENDOMETRIAL EXPOSURE TO UNOPPOSED OESTROGEN IN THE ABSENCE OF SUFFICIENT PROGESTERONE CAUSING ENDOMETRIAL HYPERPLASIA.THERE IS THREE TIMES HIGHER CHANCES OF DEVELOPING ENDOMETRIAL CANCER AND 9% LIFETIME RISK OF DEVELOPING ENDOMETRIAL CANCER vs 3% IN THE GENERAL POPULATION.
- 2) REDUCED ENDOMETRIAL RECEPTIVITY WITH NEGATIVE EFFECT ON ENDOMETRIAL AND SUBENDOMETRIAL FLOW
- 3) REDUCED GLYCODELIN IN ENDOMETRIUM CAUSING RPL
- 4) REDUCED IGF-BINDING PROTEIN THAT FACILITATES ADHESION AT MATERNAL-FOETAL SURFACE INCREASED ACUTE PHASE PROTEINS AND PRO INFLAMMATORY CYTOKINES (IL6,PIA1,TNFa) WHICH HAS NEGATIVE IMPACT ON ENDOMETRIUM AND EARLY EMBRYONIC DEVELOPMENT

## IMPACT ON IVF CYCLES

- 1) HIGHER DOSES OF GONADOTROPHINS DUE TO INCREASE IN EXOGENOUS FSH THRESHOLD BECAUSE OF GREATER AMOUNT OF BODY SURFACE, DIFFERENCES IN ABSORPTION AND METABOLIC CLEARANCE, ALTERED PERIPHERAL STEROID METABOLISM AND DECREASED SHBG LEVELS AND IMPAIRED ABSORPTION DUE TO SUBCUTANEOUS FATS.
- 2) FEWER OOCYTES COLLECTED
- 3) HIGHER CANCELLATION RATES
- 4) REDUCED PREGNANCY RATES AND LIVE BIRTH RATES.
- 5) BMI CORRELATES WITH INTRAFOLLICULAR CONCENTRATION OF THE INFLAMMATORY MARKERS IL6 AND TNF LEADING TO POOR OOCYTE QUALITY
- 6) OBESE DONOR OOCYTE RECEIPTS, REGARDLESS OF THE OOCYTE SOURCE STILL HAVE REDUCED LBR

## FACTORS CAUSING OBESITY



## HOLISTIC APPROACH TO MANAGEMENT OF OBESITY

- 1) 1<sup>ST</sup> LINE OF MANAGEMENT INCLUDES LIFESTYLE CHANGES LIKE MODIFICATION OF DIET, PHYSICAL ACTIVITY AND DAILY HABITS FOR INDIVIDUALS HAVING BMI > 25
- 2) 2<sup>ND</sup> LINE OF MANAGEMENT IS INTRODUCTION OF PHARMACOTHERAPY FOR PATIENTS WITH BMI ABOVE 27 WITH CO-MORBIDITIES AND BMI ABOVE 30 WITH NO CO MORBIDITY.
- 3) BARIATRIC SURGERY -BARIATRIC SURGERY MAY BE AN OPTION FOR TREATMENT OF EXTREME OBESITY (BMI >50)WHEN DIET AND EXERCISE IS NOT FETCHING PURPOSE.  
FERTILITY TREATMENT SHOULD BE DEFERRED UNTIL BMI IS LESS THAN 35 KG/m<sup>2</sup>

## CURRENT RECOMMENDATIONS FOR WEIGHT LOSS

- 1) LOSS OF 10% OF BODY WEIGHT
- 2) 500 TO 1000 KCAL DECREASE FROM USUAL DIET
- 3) 1 TO 2 POUND LOSS PER WEEK
- 4) SUSTAINABLE LSM

## DEVELOPMENTAL OVER NUTRITION HYPOTHESIS

PROPOSES THAT THE INCREASED FUEL SUPPLY TO THE FOETUS IN MATERNAL OBESITY OR OVERNUTRITION LEADS TO PERMANENT CHANGES IN OFFSPRING METABOLISM, BEHAVIOUR AND APPETITE REGULATION WITH RESULTANT OBESITY, METABOLIC AND BEHAVIOURAL PROBLEMS IN ADULT LIFE. SO, ONLY ACHIEVING LIFE BIRTH IN OBESE WOMEN IS NOT OUR PANULTIMATE GOAL.

## GLOBESITY

THIS IS THE FUTURE TERM AND AS HIPPOCRATES STATED-"PEOPLE OF SUCH CONSTITUTION CANNOT BE PROLIFIC. FATNESS AND FLABINESS ARE TO BLAME .THE WOMB IS UNABLE TO RECEIVE THE SEMEN AND THEY MENSTRUATE INFREQUENTLY AND LITTLE."

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